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### Absence of serological response in CF-patients colonized with *Pseudomonas aeruginosa*

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*Aims:* Aggressive treatment of early *Pseudomonas aeruginosa* (PA) infection may prevent persistent colonization. Therefore, detection of PA is of major relevance. Both culture and serological methods are used to detect PA. Our objective was to re-assess the value of serology in a large and diverse CF-population.
*Methods:* At our CF-center, we studied cultures and serology of 172 pediatric (mean age 9.90 y) and 48 adult (mean age 30.75 y) patients. Sputum- and oropharyngeal cultures taken in 2002-2004 were analyzed. We categorized patients as follows: chronic PA colonization (>50% of all cultures positive), intermittent PA colonization and negative (no positive culture). Commercially available semiquantitative IgG ELISA against 3 antigens (elastase, alkaline protease, exotoxin A) was performed on serums collected in 2004. A titer of >1:500 against one or more PA antigens was considered positive.
*Results:* We found chronic PA colonization in 42 (24%) pediatric and 25 (52%) adult patients. Sensitivity of combined antibodies for chronic colonization was 79%. Sensitivity of the individual antibody elastase was 60 %, exotoxin A 51 % and alkaline protease 54%. Negative serology occurred in 8 pediatric and 6 adult patients with chronic PA colonization. Sensitivity of combined antibodies for intermittent colonization was 33% (elastase 19%, exotoxin A 26%, alkaline protease 19%). Based on culture and serology, 73 children (42%) and 10 adults (21%) did not have evidence of PA infection during study period.
*Conclusions:* Chronically infected patients do not uniformly show an antibody response. Combining multiple antigens increases sensitivity of serology. Further investigation is needed for host- and bacterial related factors that affect antibody response.

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### Specific vaccination protects mice from lung infection with serospecific Pseudomonas aeruginosa

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*Pseudomonas aeruginosa* is an opportunistic pathogen, which is correlated closely with chronic lung infection in Cystic Fibrosis patients. Such infection is difficult to eradicate despite intensive antibiotic treatment. Therefore, prevention of *P. aeruginosa* infection by vaccination is timely desirable.
**Aim of the study:** A specific conjugated vaccine of immunotype (IT) - 4 of Lipopolysaccharide (LPS) and toxin-A (TA) was tested for its protective effect on mice suffering from chronic lung infection caused by serospecific *P. aeruginosa* 53.
**Materials & Methods:** I. Vaccine group (VG): IT-4+TA (2 μg/mouse) and Cholera Toxin (0.2 μg/mouse), control group (CG): sterile saline. II. Mice were vaccinated twice on day -28 & day -14 respectively, challenged on day 0, and sacrificed on day 5 after infection. III. Mortality, lung bacteriology, and lung pathology were evaluated after challenge. Serum immunoglobulin (Ig) G antibodies against IT-4 and TA were measured on day -28, day 0, and day 5, respectively.
**Results:** The mortality rates were 43.75% in the VG and 75.76% in the CG, the differences were significant ($p<0.01$). Serum IgG against IT-4 and TA in the VG significantly increased on day 0 ($p<0.01$ for IgG-IT4; $p<0.05$ for IgG-TA) and day 5 ($p<0.001$ for IgG-IT4; $p<0.03$ for IgG-TA) compared to CG. However, no significant difference was found in macroscopic lung pathology and lung bacteriology in both groups.
**Conclusion:** Specific vaccination with IT-4+TA conjugate significantly induces the production of IgG against IT-4 and TA in mice, and simultaneously protects mice from lethal lung infection with the serospecific *P. aeruginosa* 53 strain.

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### Vaccine failure in CF

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The prevention of influenza by vaccination represents an essential task for physicians caring for CF patients. However, because vaccines are currently not approved for children < 6 months of age, and the majority are poorly immunogenic in young children in general, vaccination is often postponed until older ages. Even the adult CF patients have not been systematically studied to determine whether they make a normal response to all vaccines and the possibility of vaccine-failure is still an unanswered issue, as reported in patients with chronic liver and renal disease. **Methods:** A total of 109 pediatric and adult patients were vaccinated against influenza in our center, during winter 2003-2004. **Results:** 2 patients showed documented vaccine failure: a 15 yrs old male and a 27 yrs old female. Influenza A CF antibody raised to 160 after vaccination, decreased again, then rose to 640 during high fever and viral symptoms 2 months after vaccination. The oldest patient showed rapid pulmonary decline and died 3 months later, 3 weeks after lung transplantation. **Discussion:** To our knowledge it is never studied if CF patients respond normally to all the vaccines and risk of vaccine failure is not documented in CF. It could be that response is reduced due to the high level of IgG in CF, also for some other vaccines. On the other hand it was never described that vaccine-preventable infections are more prevalent in CF.

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### Control and prevention of infections in cystic fibrosis patients: literature review

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We have conducted a review of the scientific literature on the following aspects pertaining to the prevention and control of infections due to classic pathogens:

- causal relationship between infection and prognosis
- transmission of germs
- risk factors for acquiring infection
- efficacy of hygienic practices in the prevention of infection

The content of the 7 most important Guidelines were compared. Over 400 papers were selected from Medline, Embase, CINHAL and the Cochrane Library, including systematic and narrative reviews, randomized and controlled trials (RCT), relevant observational studies, and congress proceedings up to December 2004. Our analysis shows that recommendations of the principal international guidelines and in general, the acquired knowledge in this field is based on observational studies, consensus and expert opinion rather than on RCT. On the basis of the examined studies, acquisition of P. aeruginosa (Pa) is associated with increased morbidity and mortality and decreased FEV1. B. cepacia complex (Bcc) further compromises FEV1 and survival. There are no demonstrable infuences on prognosis regarding MRSA, A. xylosoxidans, S. maltophilia and NT mycobacteria. The transmissibility of MRSA and non-fermentative Gram-negative bacteria has been documented. Patient cohorting seems to be efficacious in preventing transmission of Bcc and Pa, as does reduction of interpersonal contact outside hospitals and adequate hand hygiene in reducing risk of transmission.
Risk factors for acquisition of germs include external environmental factors such as sharing of respiratory devices and spaces for prolonged periods, cohabitation, summer camps, participation in educational programs, travel by car, and fitness courses.
The final synthesis of the article is a finalized report of the revision of the guidelines for infection control in Italian CF Centers and for the daily life of patients.